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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,320	05/10/2007	Noriaki Kato	868_012	4731

25191 7590 09/28/2009

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EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
09/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,320	KATO ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 - 14, 18 - 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10 - 14, 18 - 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/26/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed June 29, 2009, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Response to Amendment

1. The declaration under 37 CFR 1.132 filed June 29, 2009 is insufficient to overcome the rejection of claims 10- 12 and 14 based upon Mylari et al. (US 6,426,341) or Akita et al. (Acta Med Okayama 1993) in view of Wani et al. (JK-Practitioner 2003) as set forth in the last Office action because: the information provided does not overcome the nexus that exists between administration of SNK-860, the compound of claims 12 and 21, to diabetic patients suffering from complications of the disease.

The declaration states that there are differences between diabetic retinopathy and diabetic macular edema and that only a fraction of patients with diabetic retinopathy develop diabetic macular edema, and the diabetic population that is most likely to develop each of these conditions is different. Also stated is that aldolase reductase inhibitors such as SNK-860 disclosed in Mylari et al. have not made their way into clinical practice.

These facts are insufficient to overcome the rejections presented. The fact that the declaration and art cited therin states patients with diabetic retinopathy also develop

diabetic macular edema, with incidence rates being reported in Wisconsin Epidemiological Studies referenced by Dr. Lorenzi in his declarations, are from 3% to 20% at 10 years (Table 1, p 10, Klein et al. Ophthalmology 1995, cited on May 26, 2009 IDS) 10% to 34% over 14 years study (Table 3, p 1806, Klein et al. Ophthalmology, 1998, cited on May 26, 2009 IDS). While the clinical treatments of the conditions are not the same and the exact rate of incidence vary depending on the type of diabetes, management method employed and the length of time a patient has had diabetes, the fact that not all diabetics with retinopathy develop diabetic macular edema does not indicate that there is not a nexus between patients with diabetic retinopathy and diabetic macular edema. The end stage of the diabetic retinopathy and diabetic macular edema are not the only stage at which the two conditions should be compared – if a patient suffering from both reaches the end stage of diabetic retinopathy first, the patient will not have any vision and need not worry about blurred vision in the end stage of diabetic macular edema.

The following discussion is presented to further illustrate the point that different end stage features and treatments does not indicate that no nexus between the conditions is ever present. Kidney and ocular complications occur frequently in diabetic patients and have dramatically different outcomes at the end stage but the events that eventually lead to these dramatically different outcomes begin with diabetes. At the early stages of these conditions, treatments that ameliorate the underlying common cause of the conditions would be effective for the treatment of both kidney and ocular complications of diabetes. However, in later stages, treatments for the kidney

complications would likely not be efficacious for treating complications in the eye as at this later stage, common triggers have resulted in different cascades of events which required different interventions.

The fact that the claimed method of treatment, or other clinical treatments utilizing members of the same drug class have not been realized is not sufficient to overcome the rejections as there are many factors not relevant to the determination of patentability (e.g., the time and expense required for clinical trials to bring a treatment to the clinical setting) that can account for the failure of this class of drugs to reach the clinic.

The Examiner also notes that the claims refer to diabetic maculopathy and diabetic macular edema, while the declaration refers to diabetic retinopathy and diffuse macular edema. It is unclear whether the declaration is therefore not commensurate in scope with the instant claims or if Dr. Lorenzi is referring to the same clinical conditions using slightly different names. The central issue of this case is the particular conditions described in the cited prior art and how those conditions do or do not correlate with the conditions recited in the instant claims. The use of inconsistent terminology by Applicant in the claims, remarks and declaration without presenting a clear explanation as how these terms relate to each other means that the evidence on the record is not persuasive for withdrawal of the applied rejections.

Claim Objections

2. Claim 10 is objected to because of the following informalities: the claim does not make sense as "by the administration:" is immediately followed by the chemical formula. Appropriate correction is required.

3. Claim 18 is objected to because of the following informalities: the claim does not make sense as "inhibiting a deterioration of visual acuity in a subject" is immediately followed by the chemical formula. Appropriate correction is required.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 19 states that the method of claim 18 "further comprising improving visual acuity of the subject finally." This is not an active step that is being added to the method so it is unclear how the improved visual acuity relates to the method of claim 18. It is also unclear what is meant by the "finally" at the end of the phrase. Please clarify.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 10 – 12, 14 and 18 – 21 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Mylari (US 6,426,341). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed January 29, 2009 and those set forth herein.

In the section traversing the rejection involving Mylari et al., the teachings of a variety of references not applied in the rejection are discussed. Applicant traverses this rejection on the grounds that "prevent blindness" and "prevent and ameliorate deterioration of the visual acuity" do not mean the same thing and are different from each other in the pathological conditions. The rats, the model animal used in Akita et al., do not contain a macula lutea but a corresponding layer, while monkeys have a macula lutae. Applicants submit that no where had ARIs been tried in clinical trials for diabetic maculopathy.

These arguments are unpersuasive. Those aspects in relation to the declaration have been discussed above. In regards to the new claims 18 - 21, the active step of the method is the same as that of claims 10 - 12 and 14, namely the administration of SNK-860 to a patient with diabetic maculopathy and diffuse macular edema in an effective

amount. As the claims recite the same active step, the same results must necessarily occur as the administration of the same drug to the same patient population is being claimed. Therefore, the same effects, whether it be ameliorating diffuse macular edema (claim 10), inhibiting deterioration of visual acuity of the subject (claim 18) or improving visual acuity of the subject finally (claim 19) must occur upon administration of SNK-860.

In regards to the patient population being claimed, the arugments and evidence of the declaration are not sufficient overcome the nexus of these two eye complications occurring in the diabetic patients, the population to which Mylari et al. discloses the administration of SNK-860, also known as fiderestat. In fact, the declaration of Dr. Lorenzi indicates that a portion of the population of patients suffering from diabetic retinopathy, explicitly mentioned by Mylari et al., also have diabetic macular edema, which by implication is the same as diffuse macular edema or otherwise the declaration does not relate to the instant claims. Therefore, that subset of patients is included in the patients with complications treated by Mylari et al. and if not inherently present, it would have been obvious to one of ordinary skill to administer fiderestat to diabetic patients. Anticipation and obviousness do not require clinical practice of the method.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 10 – 12, 14 and 18 – 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akita et al. (Acta Med Okayama) in view of Wani et al. (JK

Practitioner 2003). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed January 29, 2009 and those set forth herein.

Applicant traverses this rejection on the grounds that "diabetic macular edema (diabetic maculopathy) is related to diabetic retinopathy and the two diseases overlap" does not indicate that these conditions are the same. The treatment of the conditions are not the same and Lopes de Faria teaches that it is important to classify the specific type (diffuse or focal) as they have different pathological processes.

These arguments are unpersuasive. Those aspects in relation to the declaration have been discussed above. In regards to the new claims 18 - 21, the active step of the method is the same as that of claims 10 - 12 and 14, namely the administration of SNK-860 to a patient with diabetic maculopathy and diffuse macular edema in an effective amount. As the claims recite the same active step, the same results must necessarily occur as the administration of the same drug to the same patient population is being claimed. Therefore, the same effects, whether it be ameliorating diffuse macular edema (claim 10), inhibiting deterioration of visual acuity of the subject (claim 18) or improving visual acuity of the subject finally (claim 19) must occur upon administration of SNK-860.

The last paragraph of Wani (p 277) indicates that "macular edema is the first and dominant sign of maculopathy" and does not indicate that these conditions are exactly the same. That teaching, along with the indication by Dr. Lorenzi that a fraction of patients with diabetic retinopathy develop diabetic macular edema and the Wisconsin Epidemiologic Studies of Diabetic Retinopathy cited therein indicate a nexus of diabetic

maculopathy and diabetic macular edema in diabetic patients. Akita et al. clearly demonstrates that administration of SNK-860 inhibited the abnormal changes that were observed in the eye of the diabetic rat model used. Thus, one of ordinary skill would be motivated to administer SNK-860 to diabetic patients who are either at risk of or who are already suffering from retinal complications as a result of diabetes. As the administration of SNK-860 to a specific subset of the patient population disclosed by Wani et al. and Akita et al., the same active step as the instant claims, the same outcomes must necessarily occur.

The confusion over the various conditions and how they can or cannot be used interchangeably persists, and Applicants seem to indicate diabetic macular edema and diabetic maculopathy are equated by at least some in the art (p 8, ln 7 of response). With this confusion as applied to the cited art and the conditions discussed by Dr. Lorenzi in his declaration, the evidence on the record is not sufficient to persuasively argue for withdrawal of the rejection.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

NMW